Weak Inhibitory Behavioral Effects of Postnatal/Preweaning Taurine Injections in Rats

MICHAEL A. PERSINGER
PAUL M. VALLIANT
HERMAN FALTER
Psychochemistry Lab
Departments of Psychology and Chemistry
Laurentian University
Sudbury, Ontario, Canada

The behavior of rats injected once every 2 days between Postnatal Days 4 and 20 with 62.5 μg/g or 125 μg/g body weight of taurine was compared with saline- or .5 M NaCl-injected litter-mate controls. Taurine-injected rats ran significantly less in the running wheel test and displayed lower response/reinforcement ratios following step-like changes in DRL reinforcement schedules. The quicker adjustments to the changes in DRL schedules did not occur immediately but during sessions following the change. We concluded that taurine administration during early juvenile development could weakly influence adult inhibitory behavior.

Taurine is one of the most concentrated amino acids in the rat brain yet its functions are not well understood. Taurine can readily cross the blood-brain barrier (Peck & Awapara, 1967), and according to Davison and Kaczmarek (1971) this amino acid could be an inhibitor transmitter or modulator. The possibility that both taurine and GABA (γ-amino butyric acid) share the same or similar synthesizing enzymes (Agrawal, Davison, & Kaczmarek, 1971) has fascinating implications for concepts of modulator-transmitter control systems in the central nervous system (CNS). Behavioral effects, studied only recently, suggest a weak but consistent inhibitory influence of taurine upon ambulatory and seizure-related behaviors (Baskin, Hinkamp, Marquis, & Tilson, 1974; Mutani, Bergamini, Fariello, & Delsedime, 1974; Van Gelder, 1972). Urquhart, Perry, Hansen, and Kennedy (1974) have suggested that large doses of taurine might be used to treat certain CNS disorders in that gross side effects have not been reported.

The effects of taurine administration during postnatal development, when the CNS is still plastic, have not been investigated. Consequently, we decided to study the long term behavioral effects of taurine injection during postnatal development. Although inhibition of taurine circuits was initially more preferable, such intervention is difficult and would involve undesirable side effects in other chemical systems. Behavioral tests were conducted to determine the types of behavior influenced by preweaning taurine injections. Previous experiments (M. A. Persinger & H. Falter, unpublished data)

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indicated that juvenile or adult rats injected with taurine once every 2 days between Postnatal Days 4 and 20 did not differ significantly from their litter-mate saline-injected controls with respect to open-field activity and alley running speed.

Method

Subjects

A total of 44 male and female Wistar rats (*Rattus norvegicus*), injected with either taurine or saline solutions once every 2 days between Postnatal Days 4 and 20, were used as subjects. The taurine-injected rats and their saline-injected litter-mate controls were randomly selected from 17 different litters that were delivered over a 2-yr period.

Running Wheel Experiment. Eight male and 7 female taurine rats and 8 male and 7 female controls, from 10 different litters, 75 days of age at the beginning of the experiment, were used as subjects. Eight of the taurine-control pairs were naive; the others had received open-field experience.

Reinforcement Schedule Test. Seven naive taurine-injected male rats and 7 saline-injected litter-mate controls, between 100 and 200 days of age and selected from 7 different litters, were used as subjects in an operant task with a schedule for differential reinforcement for low rates of responding (DRL).

Apparatus

Standard Lafayette Company running wheels (35 cm in diameter) were used for the running wheel test. Single-lever operant chambers (Lafayette Unit 85,000) housed in white-noise chambers with programming equipment in an adjacent room were also used.

Procedure

Injection of Subjects. Within 48 hr of birth, litters were reduced to 8 pups. On Postnatal Day 4 the pups were removed individually from the nest and injected interperitoneally (i.p.) with .5 M taurine (62.5 μg/g or 125 μg/g body weight), physiological saline, or .5 M NaCl (ionic strength of taurine). The dosage volumes for the 2 taurine concentrations corresponded to 1 μliter/g or 2 μliter/g of solution. Control materials were administered in similar dosage volumes. Subjects were injected (with a μliter syringe, 26-gauge needle) once every 2 days until Day 20.

In any given litter, 4 of the pups received taurine; the other 4 received 1 of the saline solutions. Handling and weighing of pups before injections were done as routinely and consistently as possible. Following an injection, a subject was kept in a temporary nest until all members of the litter had been weighed and injected; the litter was then returned intact to the mother. One day following the last injection the subjects were weaned and placed in housing cages where they were segregated according to gender and condition.

Identification between taurine- and saline-injected pups was maintained by coloring the dorsal surface of the pups with either a red or black marker after each injection.

The condition (taurine or saline) which received the identification mark was alternated with each liter to compensate for possible differential mothering effects. Wood shavings were used as absorbent material in the cages during the injection period. Ambient temperature averaged 21 ± 1°C. Mothers were fed Purina rat chow and water *ad libitum*. A 13-hr light: 11-hr dark cycle was used throughout the experiment.

Running Wheel Test. Low dose (62.5 μg/g body weight) taurine subjects and controls were tested 60 min per day in the running wheel for 4 consecutive days. The total number of wheel turns for each rat was recorded at the end of the test period. Tests were conducted in a lighted experimental room. Because the running wheels were housed together, 4 to 5 subjects were tested simultaneously at any given time. Tests were conducted between 1800 and 2200 hours (end of colony room's normal day cycle). Subjects were run in 5 different replications between November 1972 and April 1973.

DRL Testing. Subjects that had been injected with taurine and their litter-mate controls were gradually reduced to 80% body weight over a 14-day period. After 2 days with continuous reinforcement (CRF) training, the rats were placed on a DRL 6-sec reinforcement schedule. When the subjects had adapted to the new demand which required about 2 weeks of daily 30-min sessions, a new procedure was instituted. On what was called "step day" the demand for each animal was suddenly changed half-way through the usual 30-min session from a DRL 6-sec to a DRL 9-sec (Persinger, Lafrenière, & Ossenkopp, 1974). Total responses and reinforcements were recorded before and after the schedule changes. Following a further adaption period (about 2 weeks), a similar step was made from DRL 9-sec to DRL 12-sec. All rats were tested daily for 30 min between 0800 hours (beginning of normal day light cycle) and 1300 hours, during which time responses and reinforcements were recorded. Postsessional measurements were made for the number of fecal boluses eliminated in the chamber. Subjects were tested in 3 replications between September 1973 and May 1974.

Results

The mean numbers of wheel turns over the 4 test days for the 15 taurine male and female rats were 234 ± 117, 253 ± 144, 310 ± 163, and 380 ± 226, whereas the 15 litter-mate controls averaged 271 ± 114, 331 ± 157, 437 ± 197, and 460 ± 220. A repeated 2-way analysis of variance showed no significant treatment effect ($F = 1.58$, $df = 1/28$, $p > .05$). Because the running wheel measure was associated with high score variability, a nonparametric median test was applied to the data. The median test demonstrated that significantly more taurine-injected rats displayed fewer turns (relative to the combined group median) than the controls ($\chi^2 = 8.57$, $df = 1$, $p < .01$). Efficiency ratios for the DRL schedule for each rat for each session were calculated by dividing the total number of responses emitted by the total number of reinforcements received. Figure 1 shows the mean efficiency ratios for low dose (62.5 μg/g/48 hr) taurine animals (n = 5), low dose saline animals (n = 5), high dose (125 μg/g/48 hr) taurine animals (n = 2), and high dose controls (n = 2). A repeated measure analysis of variance demonstrated a significant treatment difference between the combined taurine groups and the control groups ($F = 5.68$, $df = 1/12$, $p < .05$). Independent t-tests for daily differences indicated that the taurine (n = 7) subjects

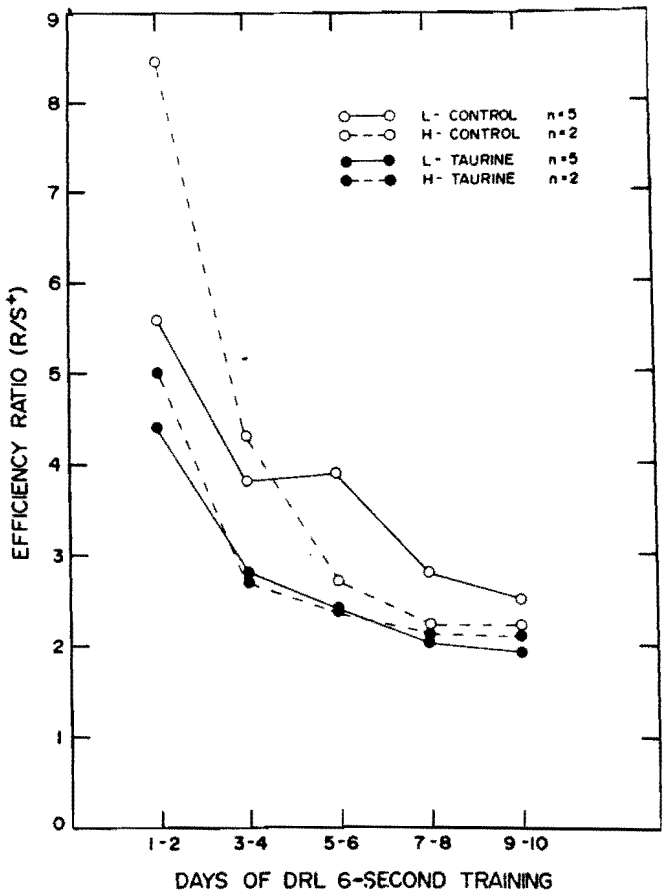

Fig. 1. Efficiency ratios during the first 10 days of DRL 6-sec testing for adult male rats that had been injected on Postnatal Days, 4, 6, 10, 12, 14, 16, 18, and 20 with taurine (L = 62.5 μg/g or H = 125 μg/g) or saline solutions.

were most significantly different from their controls (n = 7) on Days 7-8 and 9-10 (t = 2.98, t = 2.39, $p < .05$). This effect was due primarily to the decreased response perturbations following the step changes within the taurine group. Sample adjustment curves for a taurine rat and its litter mate control are shown in Figure 2. Transient adjustment scores (mean ratios of increased response/reinforcement ratios during the 15 min following the step changes)were not significantly different between groups ($t <$ 1). No differences in chamber defecation were apparent.

Discussion

Injections of taurine during early juvenile development until weaning can be associated with decreased running wheel activity and facilitated adjustment to DRL schedules. Both effects are compatible with the hypothesis that taurine may be a weak CNS inhibitor modulator. However the effect, although significant, was quite weak;

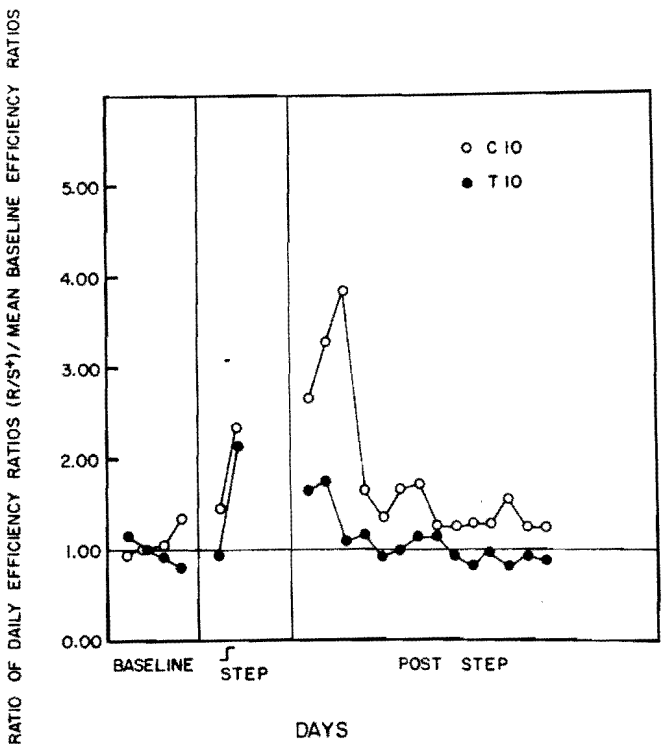

Fig. 2. The ratios of daily efficiency ratios to mean baseline ratio during baseline, step (DRL 6- to 9-sec), and post-step days for a rat (T10) that received postnatal taurine injections (62.5 μg/g/48 hr) in comparison with its litter mate control (C10).

maximum differences between taurine and control groups in both test situations ranged from 25-30%.

Whether preweaning administration of taurine permanently elevates brain taurine or whether the elevation is transient but results in morphological changes in the developing brain is not clear. Unpublished studies by H. Falter, M. A. Persinger, and G. F. Lafrenière showed no significant differences between 30-day-old taurine-injected rats and their litter-mate controls with respect to: (1) taurine levels in the cerebrum (4.4 μmole/g and 4.0 μmole/g, respectively) or cerebellum (5.1 μmole/g and 3.6 μmole/g, respectively), and (2) cellular architecture of either cortices. However, these measures may be too gross to reflect behavioral-relevant changes in that extraordinarily high concentrations of taurine (e.g., 100 μmole/g) have been reported in localized tissue, e.g., neurohypophysis (Crabai, Sitzia, & Pepeu, 1974).

Notes

Request reprints from: Dr. Michael A. Persinger, Environmental Psychophysiology Laboratory, Department of Psychology, Laurentian University, Sudbury, Ontario, Canada.

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